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Purpose: This paper presents case reports of 3 related females with varying presentations of partial ornithine transcarbamylase (OTC) deficiency and illustrates the value of earlier diagnosis of urea cycle disorders (UCDs) in asymptomatic patients.

Key takeaways:

Patient 1 (index case) is a 20-year-old female who suffered 2 incidents consistent with hyperammonemic crisis before being diagnosed with a UCD.

- During her first incident at age 12, she presented with symptoms commonly seen in patients with UCDs (lethargy, confusion, and vomiting) and resulted in hospitalization. The patient was diagnosed with food poisoning; there was no test for ammonia or a urea cycle defect.
- Between incidents, she suffered headaches and recurrent unexplained bouts of vomiting, and spontaneously became a vegetarian, which is indicative of protein avoidance.
- During her second incident at age 20, she presented with myalgia and speech disorder after experiencing rhinitis, and then hospitalization with seizures 10 days later, the latter of which was treated with valproate, an anti-convulsant known to increase plasma ammonia levels.
  - Patient experienced coma with a plasma ammonia of 510 µmol/L (normal range, 14-38 µmol/L).
  - A UCD was confirmed biochemically and the patient stabilized following dialysis and administration of nitrogen scavengers.
  - One month after being discharged from the hospital, she experienced seizures and neuropsychological sequelae, with disorders of oral understanding and expression, decreased verbal fluency, and recent and long-term memory deficiency; OTC mutation confirmed by genetic testing.

Patient 2 is the 52-year-old mother of Patient 1, who was asymptomatic until her second pregnancy.

- Developed atypical migraine headaches associated with vomiting and spontaneously chose a low-protein diet.
- Biopsy taken during a hospitalization at age 40 may have instigated 3 days of unexplained coma and 1 month of confusion and transient hypotonia.
- An acute protein loading test (following diagnosis of a UCD in Patient 1) showed that ammonia increased from 33 (baseline) to 210 µmol/L, resulting in a diagnosis of this patient as a symptomatic UCD carrier.

Patient 3 is the 28-year-old sister of Patient 1, who was asymptomatic.

- Experienced hyperammonemia (88 µmol/L) during combined protein and allopurinol-loading test administered after diagnosis of a UCD in Patient 1.

Conclusions:

- Genetic analyses found the same OTC mutation in all 3 patients, highlighting the variability of presentation that can occur with partial OTC deficiency.
- Earlier diagnosis of UCD may have stopped risky treatments administered to Patients 1 and 2 and prevented the severe consequences suffered by Patient 1.
- UCD diagnosis for Patient 3 should allow her to effectively prevent potential hyperammonemic crises.